rendered it defective. Applicants have filed a new oath/declaration herewith.

THE DRAWINGS

The Examiner has objected to the drawings contending that Figure 2 is skewed and Figure 5 should be divided into two parts. Accordingly, applicants have provided herewith replacement Figure 2 and Figure 5A/5B.

OBJECTIONS TO THE SPECIFICATION

The Examiner has objected to the Specification based on a number of informalities. Applicants have amended page 9 to correct spacing, page 18 to correct a handwritten notation, page 19 to correct a misspelled word, pages 26, 28, 29, 30, 31 to remove an extra comma, page 33 to correct a typographical error, and to remove a comma and an extra space, page 34 to add a space, page 35 to remove a comma and correct capitalization, page 45 to correct a typographical error and page 57 to delete an extra line. The applicants have amended the specification as requested by the Examiner. Accordingly, applicants request that the outstanding objections be withdrawn.

CLAIM OBJECTIONS

The Examiner has objected to claim 9, contending that the claim repeats the word "least". Applicants have amended claim 9 to remove this repetition.

Accordingly, applicants request that the outstanding objections be withdrawn.

THE REJECTIONS

35 U.S.C. § 112, first paragraph

Claims 1-21 and 43-56 stand rejected under 35 U.S.C. § 112. Specifically, the Examiner contends that "the specification, while being enabling for an isolated cell culture of GFAP+ cells wherein the proliferation-inducing factor is epidermal growth factor (EGF), does not reasonably provide enablement for any other proliferation-inducing growth factor." Office Action, page 4. The Examiner further contends that the specification does not describe the "[s]pecific biological actions/activities that the proliferation-inducing factors would affect. Office Action, page 5.

Finally, the Examiner contends that a large amount of experimentation is necessary to identify all the applicable growth factors. Applicants traverse.

The present inventors have discovered that GFAP expressing cells can differentiate into neurons upon withdrawal of growth factor and serum from the medium. Therefore, although the proliferation-inducing factor is required for growing the cell culture prior to differentiation, it is not necessarily the inventive concept on which the claims are based. Accordingly, elucidation of the specific biological activities affected by proliferation-inducing factors is unnecessary to the practice of the invention. Further, and in this respect, the Examiner's contention that "a large amount of experimentation would be required to identify all applicable growth factors" is inaccurate. The Federal Circuit held in In re Wands that the necessary screening of a large number of negative hybridomas does not render the field unpredictable because "practitioners of this art are prepared to screen negative hybridomas in order to find one that makes the desired antibody." In re Wands at 1406. Similarly, practitioners in the field of cell culture are prepared to screen growth factors in order to find those that produce the desired effect. This is even more true when practitioners are given the level of guidance imparted by applicants' disclosure and the clear objectives defined therein.

Applicants respectfully request that the Examiner withdraw the outstanding written description rejection.

35 U.S.C. § 112, second paragraph

Claims 2, 4, 7, 44, 46, 48, 50, 51, 53, and 55 stand rejected under 35 U.S.C. § 112, second paragraph as being "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention."

Specifically, the Examiner contends that claims 2, 4, 7, 44, 46, 48, 50, 51, 53, and 55 are vague in reciting the term "majority". Office Action, page 6. Applicants have obviated this rejection by amending the rejected claims to recite "greater than 50%" instead of "the majority". Such language is consistent with the plain meaning of the term.

The Examiner contends that claims 18 and 21 are indefinite as to the meaning of the term "some". Applicants have amended the claims to recite the phrase "at least a portion" in place of

"at least some" thus obviating the rejection.

The Examiner contends that claims 1-23 are indefinite because the metes and bounds of the terms "proliferation-inducing growth factor" and "differentiation-inducing culture conditions" are not adequately defined in the specification. Applicants traverse.

As an initial matter, the two terms are defined in the specification, for example, on page 12, line 9 onward. Additionally, the same or equivalent terms are used in the claims of the very same patent documents cited by the Examiner (i.e. U.S. 5,750,376 – claims 1, 24, 30; U.S. 6,497,872 – claims 1 and 22). Accordingly, the terms are established and understood in the art.

35 U.S.C. § 102(b)

Claims 1-23 and 43-56 stand rejected under 35 U.S.C. § 102(b). Specifically, the Examiner contends that United States Patent No. 5,753,506 teaches "an *in vitro* adhesion culture of CNS stem cells from a mammal." Applicants traverse.

The present inventors have discovered that GFAP expressing cells can proliferate and differentiate into neurons under certain *in vitro* conditions by withdrawal of growth factor and serum from the medium. The cells have a glial morphology and, in addition to GFAP, they express nestin during proliferation (page 6, lines 16-20). In this way, a reliable source of large numbers of neural cells has been provided for the various uses contemplated by the present inventors.

US 5,753,506 discloses methods for expansion of CNS stem cells and differentiation of these into neurons, oligodendrocytes and astrocytes. The reference does **not** disclose that the stem cells capable of expansion and differentitation express GFAP and nestin. In contrast, it it expressly stated that cells only express GFAP and Nestin **after** differentiation. See e.g. column 14 which is entitled "**Differentiation** and Analysis of CNS Stem Cells from Embryonic Rat Brain". Lines 36-48 clearly state that the cells expressing GFAP were glial cells appearing 6 days after differentiation. In the context of US 5,753,506, GFAP is considered a glial marker so it it not surprising that glial cells express it.

Importantly, US 5,753,506 does not disclose GFAP and Nestin expressing cells that can expand and in turn differentiate into neurons. GFAP is a glial marker and it reads in column 13,

lines 45-49 that cells exhibiting glial characteristics (i.e. that express GFAP) have lost their multipotential capacity and are unable to differentiate into neurons. The skilled person thus learns from US 5,753,506 that cells that express GFAP (and Nestin) are differentiated glial cells that have lost their capacity to differentiate into other cell types. Therefore, US 5,753,506 does not teach an *in vitro* adhesion culture of GFAP+ cells that can differentiate into neurons and does not teach a cell culture comprising at least 90% $GFAP^+$ cells as recited in applicants' amended claim 1. Similarly US 5,753,506 does not teach an *in vitro* cell culture with cells that are GFAP+ and can differentiate into neurons (claim 3). US 5,753,506 also does not teach a method of producing a neuronal cell from a GFAP+ cell (claim 22). Finally, US 5,753,506 does not teach a cell population consisting essentially of isolated GFAP+ nestin+ cells as US 5,753,506 does not disclose co-expression of these two markers (claim 42).

CONCLUSION

Applicant respectfully requests that the Examiner enter the requested amendments, consider the foregoing remarks and withdraw the outstanding rejections. Should the Examiner feel that a telephone conference would expedite allowance of the pending claims, she is invited to call the undersigned.

Respectfully submitted,

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